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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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KIRKPATRICK & LOCKHART NICHOLSON GRAHAM LLP
535 SMITHFIELD STREET
PITTSBURGH, PA 15222

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,326	GODFREY ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60,61,63,64,78-86 and 105-171* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *78-86,112 and 113* is/are allowed.

6)☒ Claim(s) *60,63,105,109,114-119 and 147* is/are rejected.

7)☒ Claim(s) *61, 64,106-108,110,120-146 and 148-171* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAIL ACTION

1. Applicant's amendment filed May 9, 2005 is acknowledged and has been entered. Claims 60, 78, 79, 82-86 have been amended. Claims 105-171 have been added. Claims 1-59, 62, 65-77, 87-104 have been canceled. Claims 60, 61, 63-64, 78-86 and 105-171 are pending. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The previous rejections under 35 USC 102(b) are withdrawn in view of Applicant's cancellation of the claims.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 11: New Matter Rejection

4. Claims 119 and 147 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation "wherein one or both primers of the second primer set do not anneal to an amplicon product produced by the first primer set in the PCR amplification" is not

supported by the specification as originally filed. Nowhere in the specification is there a recitation of the negative *proviso* recited in the claims 119 and 147. The specification discloses at paragraph 0009 that:

"...the second primer set is added to the reaction mixture at the beginning of the second amplification stage, thereby limiting the physical presence of the second primer set during the first stage. In this method, the rarer target sequence preferably is amplified before the less-rare sequence which typically is a control, such as .beta.-gus or 18SrRNA sequences".

There is nothing in that disclosure or anywhere else in the specification which recites or suggest that "one or both primers of the second primer set do not anneal to an amplicon product produced by the first primer...". Based on the lack of support of instant invention as recited in claims 119 and 147, the specification would not have suggested to the skill artisan that the Applicant was in possession of the claimed invention as of the filing date of the application.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 60, 63, 105 and 115-118 are rejected under 35 U.S.C. 102(b) as being anticipated by Takano et al. (The journal of Clinical endocrinology and Metabolism, vol. 84, No. 3, pages 951-955). Regarding claims 60 and 116, Takano et al teach a method comprising conducting a reverse transcription reaction for less than about 10 minutes on an RNA sample in a reaction mixture to produce a DNA sample; (b) adding a PCR reagent composition containing a PCR primer set and a thermostable DNA polymerase to the reaction mixture and conducting a PCR amplification on the reaction mixture (page 952, col. 2, first full paragraph beginning at line 3).

Regarding claim 63 and 117, Takano et al teach the method of claims 60 and 116, wherein the reverse transcription reaction is conducted for about 2 minutes (see page 952, col. 2, first full paragraph).

Regarding claims 105, Takano et al teach a method comprising conducting a PCR amplification reaction on a DNA sample in a PCR reaction mixture, wherein the PCR amplification is conducted in a first amplification stage and a second amplification stage, each amplification stage comprising one or more PCR cycles and each cycle comprising a denaturing step, an annealing step and an elongation step, wherein the PCR amplification of the second amplification stage is conducted under different reaction conditions than the PCR amplification of the first amplification stage and wherein the denaturation step for one or more cycles is about 1 minute or less (page 952, col. 2, first full paragraph). Takano et al further teach wherein one of the first primer and the second primer set produce a carcinoembryonic antigen-specific amplicon (same citation as above).

Regarding claim 115, Takano et al teach a method comprising conducting a PCR amplification on a PCR reaction mixture in a first stage and a second stage, the reaction mixture comprising a DNA sample, a first primer set having a first effective Tm and a second primer sect having a second effective Tm different from the first effective Tm[1], each amplification stage comprising one or more PCR cycles, each PCR cycle comprising a denaturing step, an annealing step and elongation step, wherein the annealing step of the first amplification stage is conducted at a greater temperature (60°C) than the annealing step of the second amplification stage (55°C) (page 952, col. 2, first full paragraph).

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[1] The Tm was calculated by the Examiner using the following formula:
Tm (°C) = 2x(A + T) + 4 x (G + C).

Regarding claim 118, Takano et al teach the method of claim 116, wherein the reverse transcription reaction is conducted prior to the first amplification and prior to the addition of one of PCR primers and a thermostable DNA polymerase to the reaction mixture, to produce DNA in the DNA sample of the reaction mixture (page 952, col. 2, first full paragraph).

7. Claims 105 is rejected under 35 U.S.C. 102(b) as being anticipated by Gerhard et al (Journal of Clinical Oncology, vol. 12, No. 4, pages 725-729, April 1994). Regarding claim 105, Gerhard et al teach a method comprising a PCR amplification on a DNA sample in a PCR reaction mixture, wherein the PCR amplification is conducted in a first amplification state and second amplification state, each amplification stage comprising on one or more PCR cycles and each PCR cycle comprises a denaturing step, an annealing step and an elongation step that may be conducted at the sample temperature as the annealing step, wherein the PCR amplification of the second amplification of the second amplification stage is conducted under different reaction conditions than the PCR amplification of the first amplification stage and wherein one of the first PCR primer set and the second PCR set produces a carcioembryonic antigen specific amplicon (page 726, col. 2, first full paragraph).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 109 and 114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howell et al (US 5995552, November 16, 1999) in view of Kurnit et al (US 6033854, March 7, 2000). Regarding claim 109 and 114, Howell et al teach a method comprising the steps of conducting a PCR amplification reaction on a DNA sample in a OCR reaction mixture, wherein the PCR amplification is conducted in a first amplifications stage and a second amplification stage, each amplification stage comprising one or more PCR cycles and each cycle comprising a denaturing step, an annealing step, an elongation step that may be conducted at the same temperature ad the annealing step, wherein the PCR amplification of the second amplification stage is conducted under different reaction conditions than the PCR amplification of the first stage (col. 23, line 22 to col. 24, line 16). Howell et al differs from the instant invention in that

the patent does not expressly teach wherein the amplification states include one or more quantitative PCR reactions using a fluorescent reporter molecule to indicate accumulation of a specific amplicon.

Kurnit et al teach a PCR method comprising steps similar to that of Howell et al. Kurnit et al teach wherein the method comprises carrying out a two-stage (nested) PCR reaction wherein the profile for the reaction is monitored by fluorescence using quantitative PCR conditions (col. 7, line 65 to col. 8, line 20). Kurnit et al teach that the method allows for increase specificity of the reaction product (col. 8, lines 10-20). Therefore, one of ordinary skill in the art would have been motivated at the time of the claimed invention to have modify the method of Howell et al to encompass a step of quantitative PCR for the benefits of increasing specificity of the reaction conditions as suggested by Kurnit et al.

Conclusion

11. Claims 60, 63, 105, 109, 114-119 and 147 are rejected. Claims 64, 106-108, 110, 120-146 and 148-171 are objected because they depend from rejected claims. Theses claim have not been rejected under prior art because no motivation could be found for the limitations recited therein. Claims 78-86 and 112 and 113 are free of the prior art because not prior art could be found wherein a PCR method was performed during surgery. The closest prior art not relied upon: Brown et al teach a method of detecting intraoperative tumor cell dissemination in patients with breast cancer by use of reverse transcription and PCR. The reference teaches wherein samples were collected before, during and after an operation followed by analysis via RT-PCR. Claims 112 and 113 are free of the prior art because no prior art could be found teaching a PCR

method wherein the denaturation step is carried out for 1 second or less. The closest art made of record teaches wherein the denaturation step is at least 1 minute or 30 seconds.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

CYNTHIA WILDER
PATENT EXAMINER